

Supplementary Table 1. Descriptive characteristics of acetaminophen and/or antibiotic use in the 1998 and 2003 birth cohorts, separately.

	1998 birth cohort (N = 263,620)				2003 birth cohort (N = 9,910)			
	No use of acetaminophen and antibiotics	Only antibiotics	Only acetaminophen	Use both drugs	No use of acetaminophen and antibiotics	Only antibiotics	Only acetaminophen	Use both drugs
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
<b>Sex</b>								
Female	6,209 (52.09)	8,031 (51.27)	11,044 (51.64)	100,938 (47.02)	366 (53.59)	93 (51.38)	2,174 (49.48)	2,098 (45.10)
Male	5,711 (47.91)	7,632 (48.73)	10,344 (48.36)	113,710(52.98)	317 (46.41)	88 (48.62)	2,220 (50.52)	2,554 (54.90)
<b>EC at Birth</b>								
I	1,049 (8.80)	1,549 (9.89)	2,482 (11.60)	20,678 (9.63)	63 (9.22)	9 (4.97)	396 (9.01)	410 (8.81)
II	4,797 (40.24)	7,550 (48.20)	10,271 (48.02)	98,344 (45.82)	341 (49.93)	103 (56.91)	2,310 (52.57)	2,307 (49.59)
III	2,628 (22.05)	4,224 (26.97)	5,258 (24.58)	64,136 (29.88)	135 (19.77)	40 (22.10)	1,118 (25.44)	1,359 (29.21)
IV	3,447 (28.92)	2,340 (14.94)	3,377 (15.79)	31,490 (14.67)	144 (21.08)	29 (16.02)	570 (12.97)	576 (12.38)
<b>Geographical area at birth</b>								
Urban	3,734 (31.32)	4,841 (30.91)	7,326 (34.25)	57,024 (26.57)	230 (33.67)	72 (39.78)	1,372 (31.22)	1,247 (26.81)
Suburban	6,824 (57.24)	9,443 (60.29)	12,057(56.37)	132,523(61.74)	383 (56.08)	94 (51.93)	2,514 (57.21)	2,815 (60.51)
Rural	1,160 (9.73)	1,083 (6.91)	1,522 (7.12)	21,064 (9.81)	50 (7.32)	5 (2.76)	369 (8.40)	476 (10.23)
<b>Cumulative number of ambulatory visits during the first year of life</b>								
0	4,394 (36.86)	209 (1.33)	287 (1.34)	623 (0.29)	86 (12.59)	2 (1.10)	14 (0.32)	10 (0.21)
1-6	3,604 (30.23)	1,830 (11.68)	3,432 (16.05)	6,911 (3.22)	182 (26.65)	18 (9.94)	289 (6.58)	90 (1.93)
7-12	1,958 (16.42)	3,397 (21.69)	6,095 (28.50)	23,599 (10.99)	181 (26.50)	36 (19.89)	847 (19.28)	412 (8.86)
≥13	1,965 (16.48)	10,227(65.29)	11,574(54.11)	183,515(85.50)	234 (34.26)	125 (69.06)	3,244(73.83)	4,140 (88.99)
<b>Cumulative number of inpatient visits during the first year of life</b>								
0	9,549 (80.10)	12,674(80.92)	16,743(78.28)	158,636(73.91)	572 (83.75)	143 (79.01)	3,276 (74.56)	3,066 (65.91)
1	1,973 (16.55)	2,426 (15.49)	3,757 (17.57)	40,974 (19.09)	96 (14.06)	32 (17.68)	873 (19.87)	1,075 (23.11)
2-3	354 (2.97)	500 (3.19)	795 (3.72)	13,176 (6.14)	14 (2.05)	6 (3.31)	220 (5.01)	440 (9.46)
≥4	45 (0.38)	63 (0.40)	93 (0.43)	1,862 (0.87)	1 (0.15)	- (0.00)	25 (0.57)	71 (1.53)

Supplementaey Table 2. Relationship between acetaminophen/antibiotic exposure during the first year of life and the subsequent development of asthma\*, in the two birth cohorts.

	1998 birth cohort	2003 birth cohort
	Adj_HR <sup>a,b</sup> (95% CI)	Adj_HR (95% CI)
<b>Drug exposure</b>		
Non exposure	ref	ref
Only exposure to antibiotics	<b>1.30</b> (1.19-1.43) <sup>c</sup>	1.11 (0.64-1.91)
Only exposure to acetaminophen	<b>1.39</b> (1.27-1.52)	1.04 (0.77-1.41)
Exposure to both drugs	<b>1.26</b> (1.17-1.36)	0.96 (0.70-1.32)
<b>Gender</b>		
Female	ref	ref
Male	<b>1.15</b> (1.12-1.19)	1.10 (0.96-1.26)
<b>EC at birth<sup>d,e</sup></b>		
1	ref	ref
2	0.97 (0.93-1.02)	1.08 (0.84-1.39)
3	<b>0.88</b> (0.83-0.93)	1.07 (0.81-1.42)
4	<b>0.89</b> (0.84-0.94)	0.97 (0.71-1.32)
<b>Geographical area at birth</b>		
Urban	ref	ref
Suburban	<b>0.96</b> (0.93-0.99)	1.04 (0.89-1.22)
Rural	<b>0.87</b> (0.82-0.92)	0.88 (0.65-1.19)

Note:

\* Exclude children aged from 2 to 4 years in the analysis.

<sup>a</sup> Adj\_HR is the abbreviation for adjusted hazard ratio.

<sup>b</sup> Adjusted for all the other variables listed in the Table, plus healthcare utilization (including no. of ambulatory visits, no. of inpatient visits, no. of otitis media diagnoses, and no. of bronchitis diagnoses).

<sup>c</sup> *p* value < 0.05 is bold.

<sup>d</sup> EC is the abbreviation for enrollee category.

<sup>e</sup> Higher EC category indicates lower SES level.

Supplementary Table 3. Relationship between acetaminophen/antibiotic exposure during the first year of life and the subsequent development of the three examined allergic diseases, stratified by the status of respiratory tract infection in the two birth cohorts.

<b>1998 birth cohort</b>			
	<u>Atopic dermatitis</u> Adj_HR <sup>a,b</sup> (95% CI)	<u>Asthma</u> Adj_HR (95% CI)	<u>Allergic rhinitis</u> Adj_HR (95% CI)
Subjects with diagnosed respiratory tract infections during the first year of life			
Non exposure	ref	ref	ref
Only exposure to antibiotics	0.99 (0.86-1.14)	0.94 (0.85-1.03)	0.96 (0.89-1.05)
Only exposure to acetaminophen	<b>1.16</b> (1.02-1.32) <sup>c</sup>	<b>1.12</b> (1.02-1.22)	<b>1.14</b> (1.06-1.23)
Exposure to both drugs	<b>1.15</b> (1.02-1.30)	1.08 (1.00-1.18)	1.08 (1.00-1.16)
Subjects without diagnosed respiratory tract infections during the first year of life			
Non exposure	ref	ref	ref
Only exposure to antibiotics	<b>1.67</b> (1.52-1.83) <sup>c</sup>	<b>1.38</b> (1.29-1.48)	<b>1.42</b> (1.34-1.51)
Only exposure to acetaminophen	<b>1.89</b> (1.73-2.07)	<b>1.59</b> (1.50-1.70)	<b>1.64</b> (1.55-1.73)
Exposure to both drugs	<b>2.09</b> (1.93-2.25)	<b>1.63</b> (1.55-1.73)	<b>1.70</b> (1.62-1.78)
<b>2003 birth cohort</b>			
	<u>Atopic dermatitis</u> Adj_HR (95% CI)	<u>Asthma</u> Adj_HR (95% CI)	<u>Allergic rhinitis</u> Adj_HR (95% CI)
Subjects with diagnosed respiratory tract infections during the first year of life			
Non exposure	ref	ref	ref
Only exposure to antibiotics	0.98 (0.63-1.54)	0.86 (0.62-1.19)	1.15 (0.88-1.51)
Only exposure to acetaminophen	0.92 (0.72-1.18)	1.00 (0.85-1.19)	1.12 (0.97-1.30)
Exposure to both drugs	0.97 (0.75-1.24)	1.06 (0.89-1.25)	1.16 (1.00-1.35)
Subjects without diagnosed respiratory tract infections during the first year of life			
Non exposure	ref	ref	ref
Only exposure to antibiotics	<b>4.34</b> (1.20-15.75) <sup>c</sup>	1.82 (0.71-4.66)	<b>2.83</b> (1.32-6.04)
Only exposure to acetaminophen	1.71 (0.83-3.53)	1.28 (0.78-2.10)	<b>1.65</b> (1.10-2.49)
Exposure to both drugs	2.29 (0.94-5.60)	<b>1.99</b> (1.10-3.60)	1.71 (0.98-2.98)

Note:

<sup>a</sup> Adj\_HR is the abbreviation for adjusted hazard ratio.

<sup>b</sup> Adjusted for gender, enrollee category at birth, geographical area at birth and healthcare utilization (including no. of ambulatory visits, no. of inpatient visits).

<sup>c</sup> *p* value < 0.05 is bold.